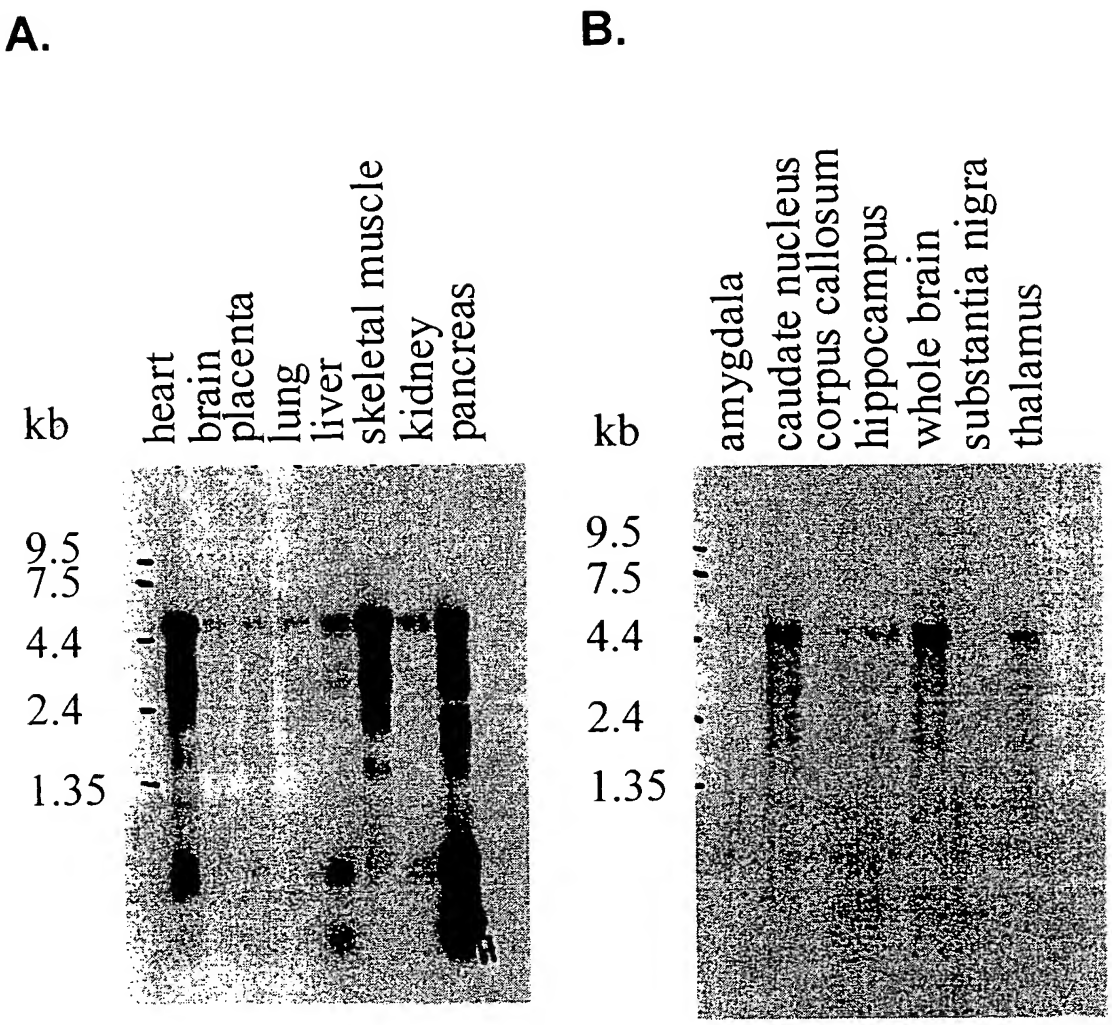


Figs. 1A and 1B

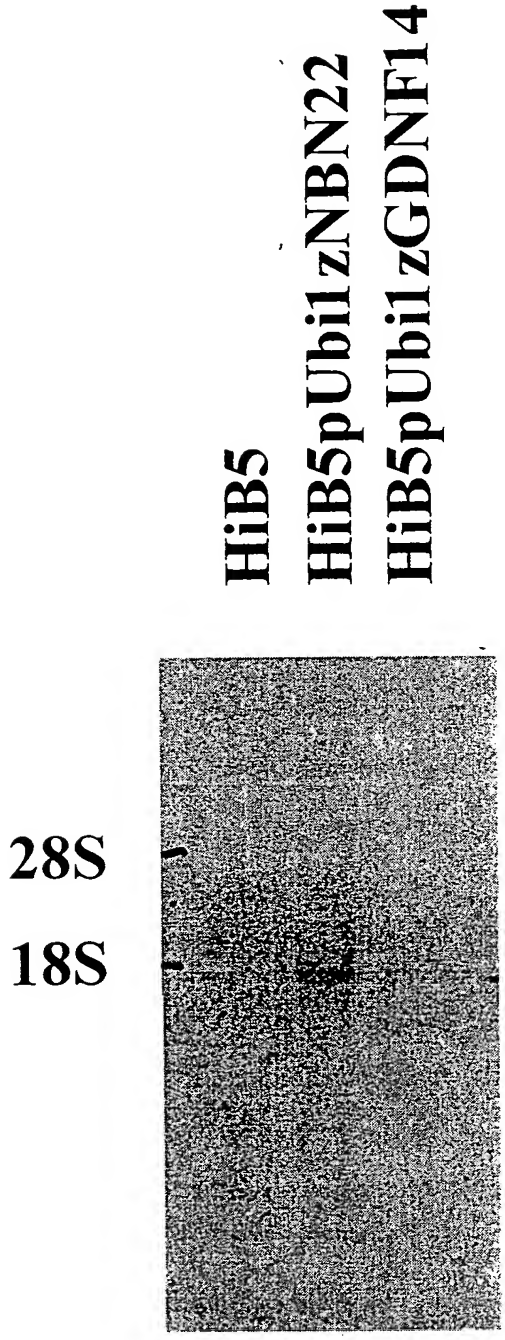


Fig. 2

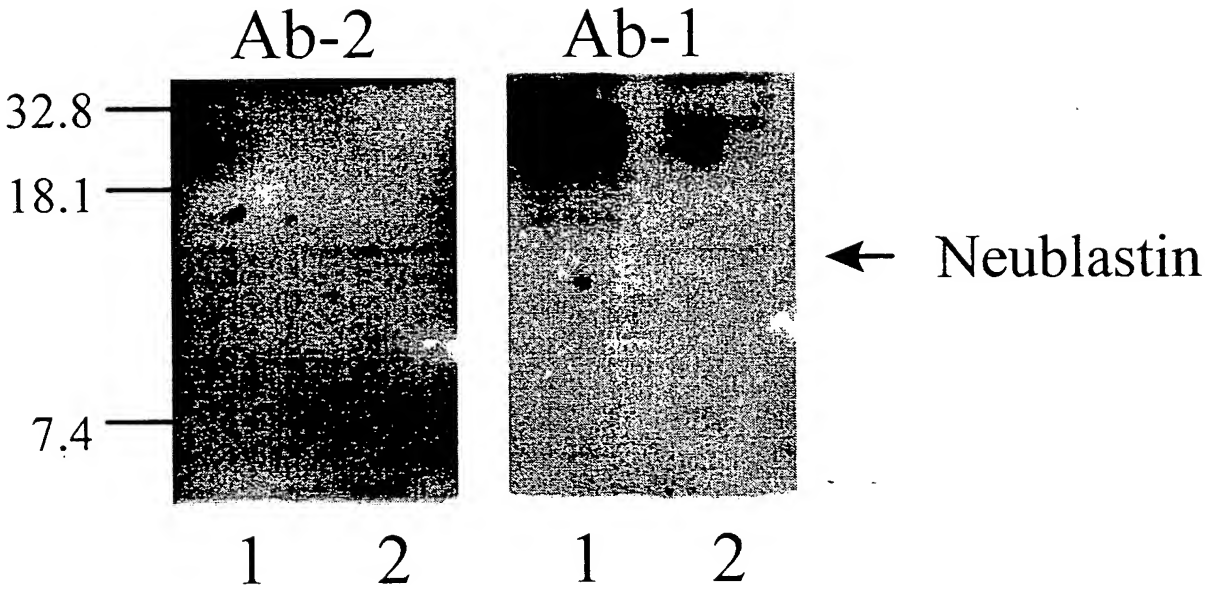
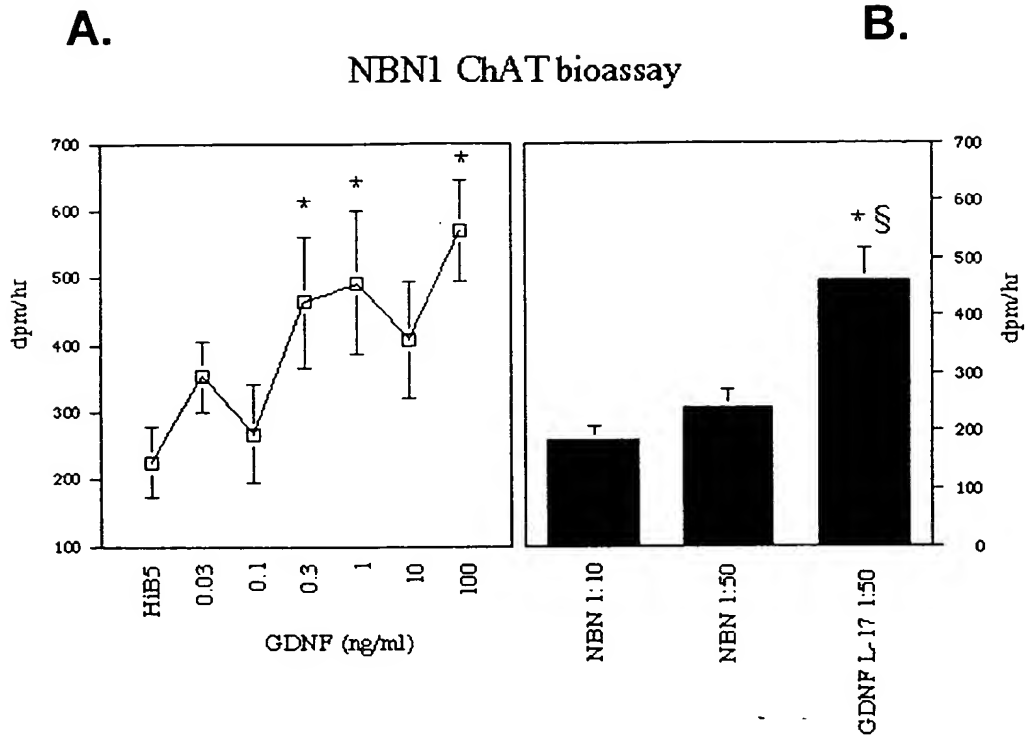
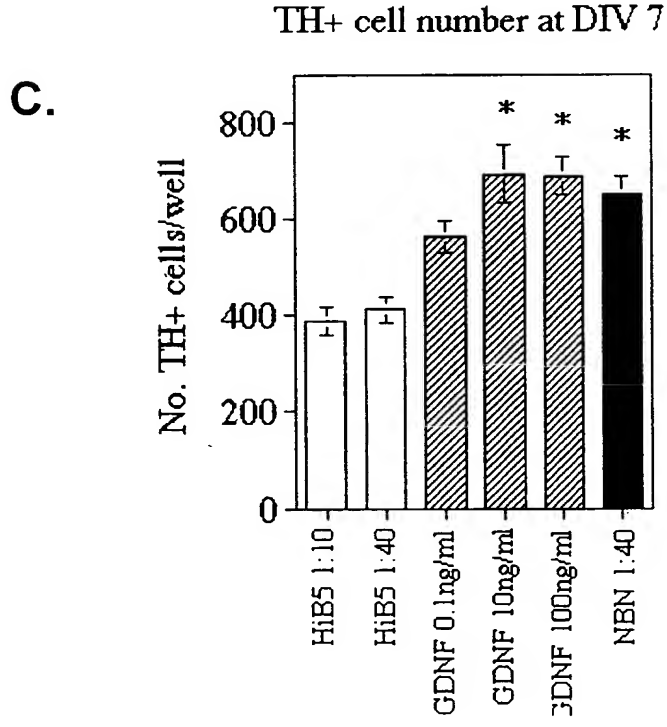
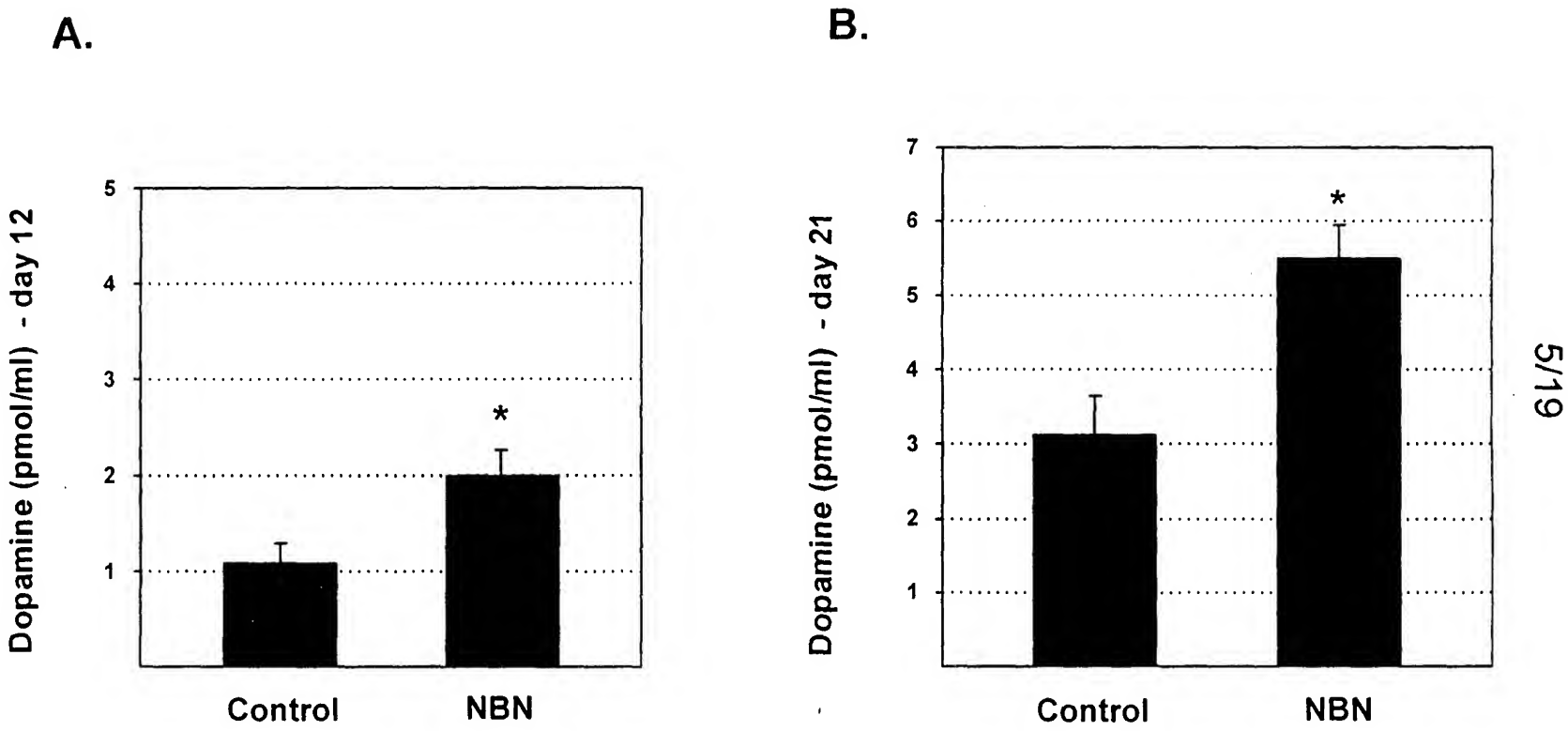


Fig. 3





Figs. 4A, 4B and 4C



Figs. 5A and 5B

C.

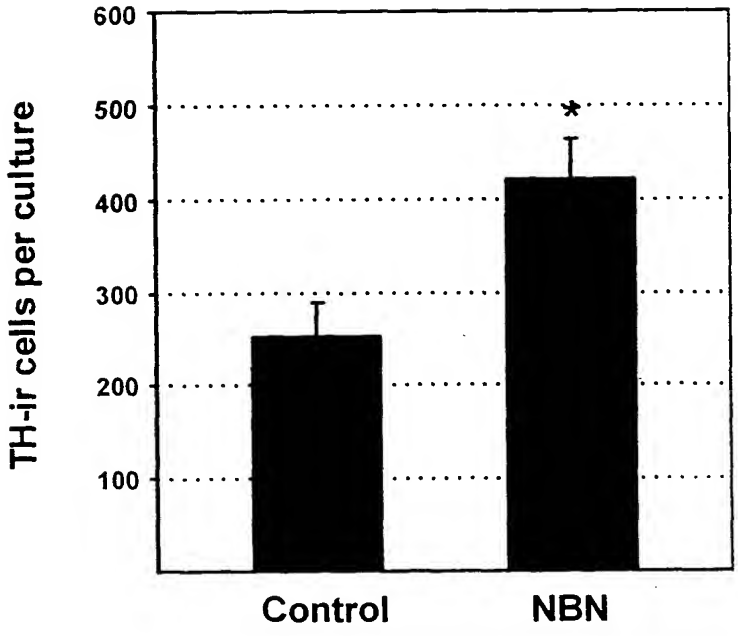


Fig. 5C

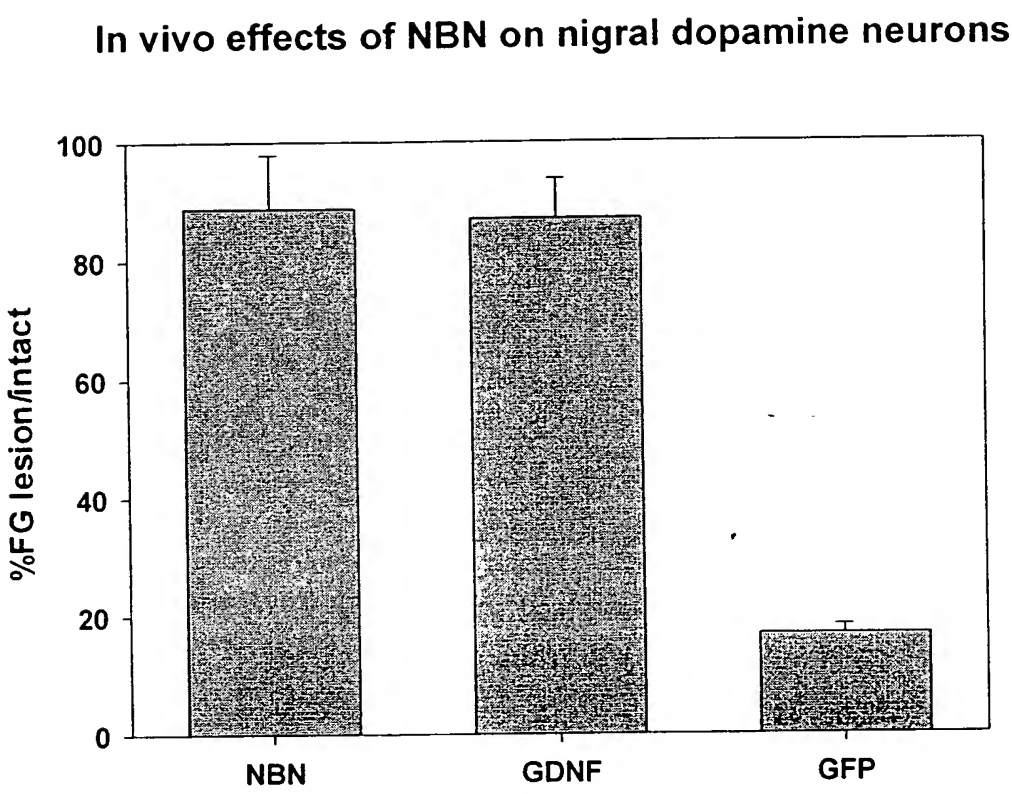
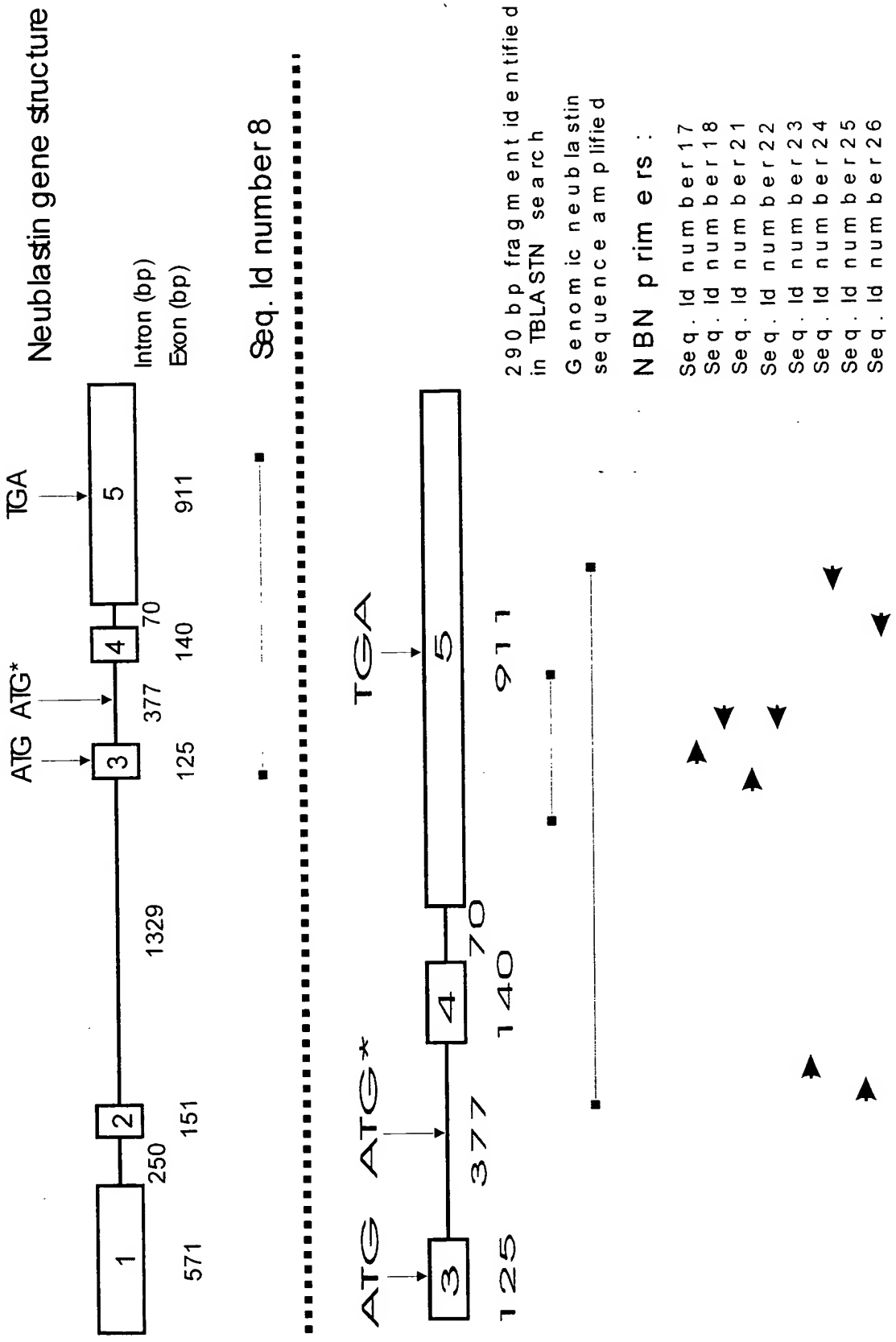

In vivo effects of NBN on nigral dopamine neurons
%FG lesion/intact
100
80
60
40
20
0
NBN
GDNF
GFP

Fig. 6

FIG. 7


Neublastin gene structure
Intron (bp)
Exon (bp)
Seq. Id number 8
TGA
ATG
ATG*
1
2
3
4
5
571
250
151
1329
125
377
70
140
911
290 bp fragment identified in TBLASTN search
Genomic neublastin sequence amplified
NBN primers :
Seq. Id number 17
Seq. Id number 18
Seq. Id number 21
Seq. Id number 22
Seq. Id number 23
Seq. Id number 24
Seq. Id number 25
Seq. Id number 26

Alignment of Neublastin primers used in Rapid-Screen with homologous regions in other GDNF ligands

5′-**C CTG GCC AGC CTA CTG GG**-3′	**SEQ ID No 17**	
G **CTG GCC CGG CTG CAG GG**		persephin
G **CTG** CGA CGA **CTG** CGC CA		neurturin
A **TTG** AAA AAC **TTA** TCC AG		GDNF

5′-**AA GGA GAC CGC** **TTC GTA GCG**-3′	**SEQ ID No 18**	
TA GGC CAC GTC GGT **GTA GCG**		persephin
AA GGA CAC CTC GTC **CTC GTA GGC**		neurturin
AA CGA CAG GTC ATC **ATC** AAA GGC		GDNF

conserved nucleotides shown in **bold**

Fig. 8

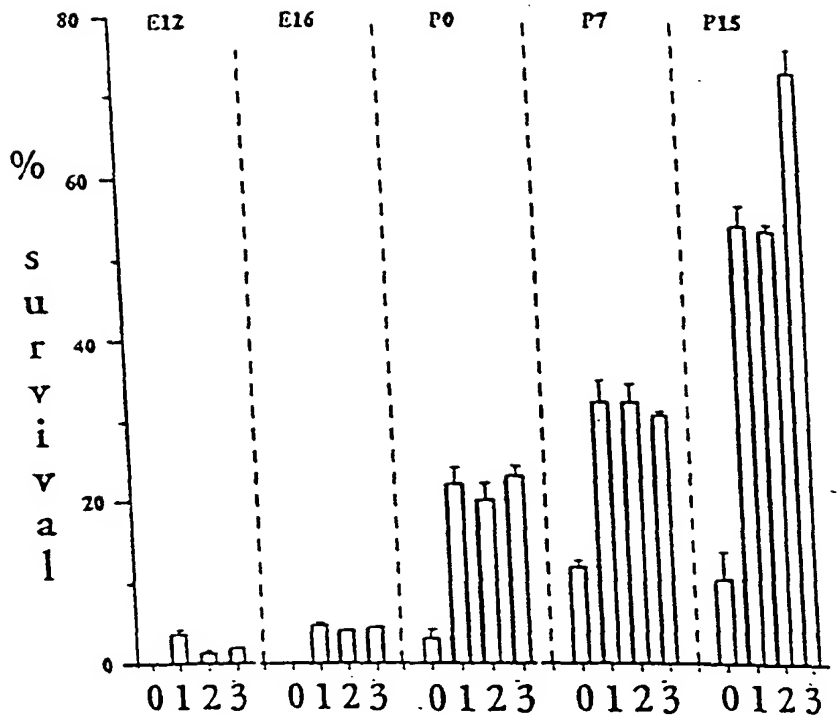

80
60
40
20
0
% survival
E12
E16
P0
P7
P15
0123 0123 0123 0123 0123

Fig. 9

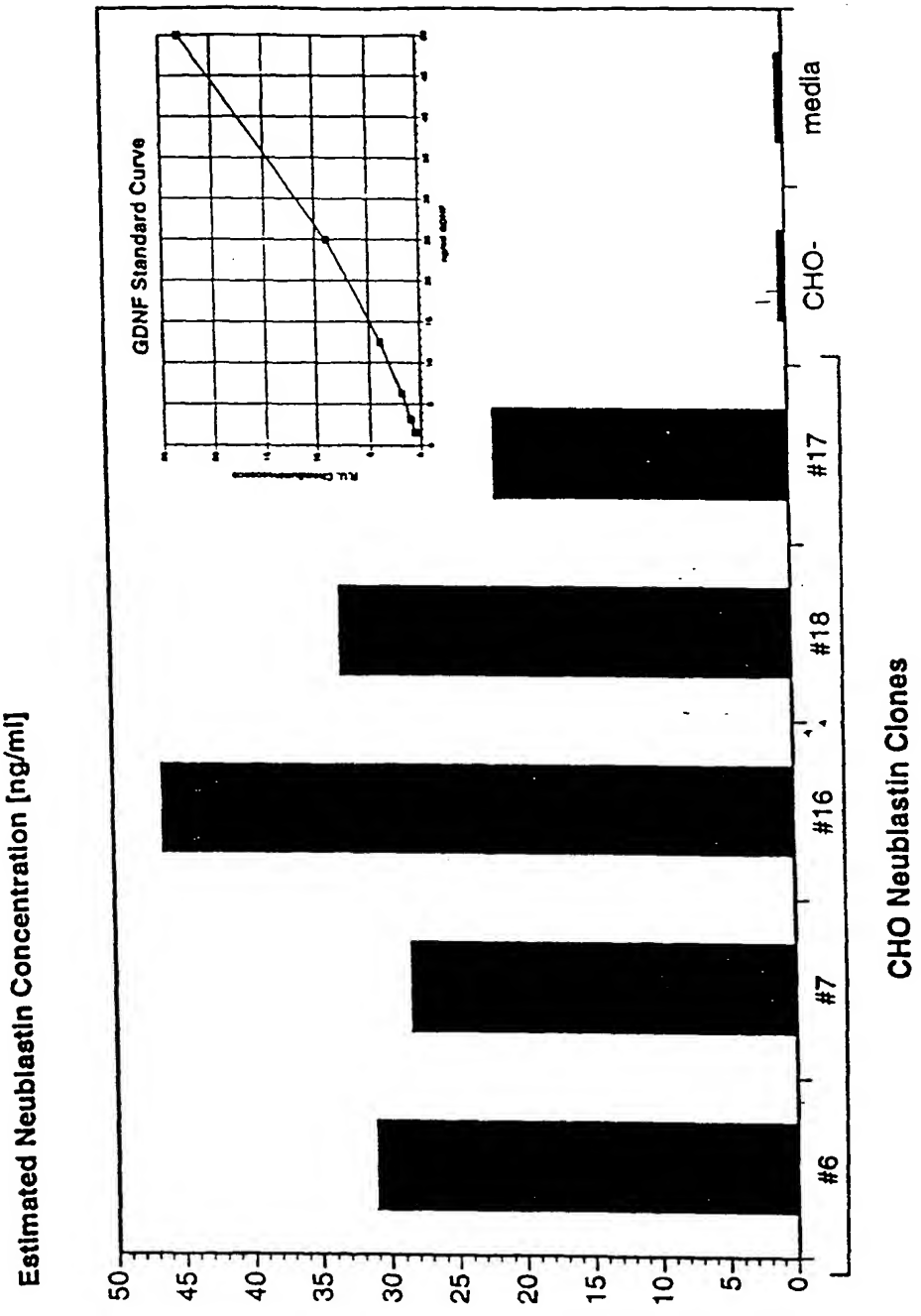

GDNF Standard Curve
Estimated Neublastin Concentration [ng/ml]
0
5
10
15
20
25
30
35
40
45
50
#6
#7
#16
#18
#17
CHO-
media
CHO Neublastin Clones

Fig. 10

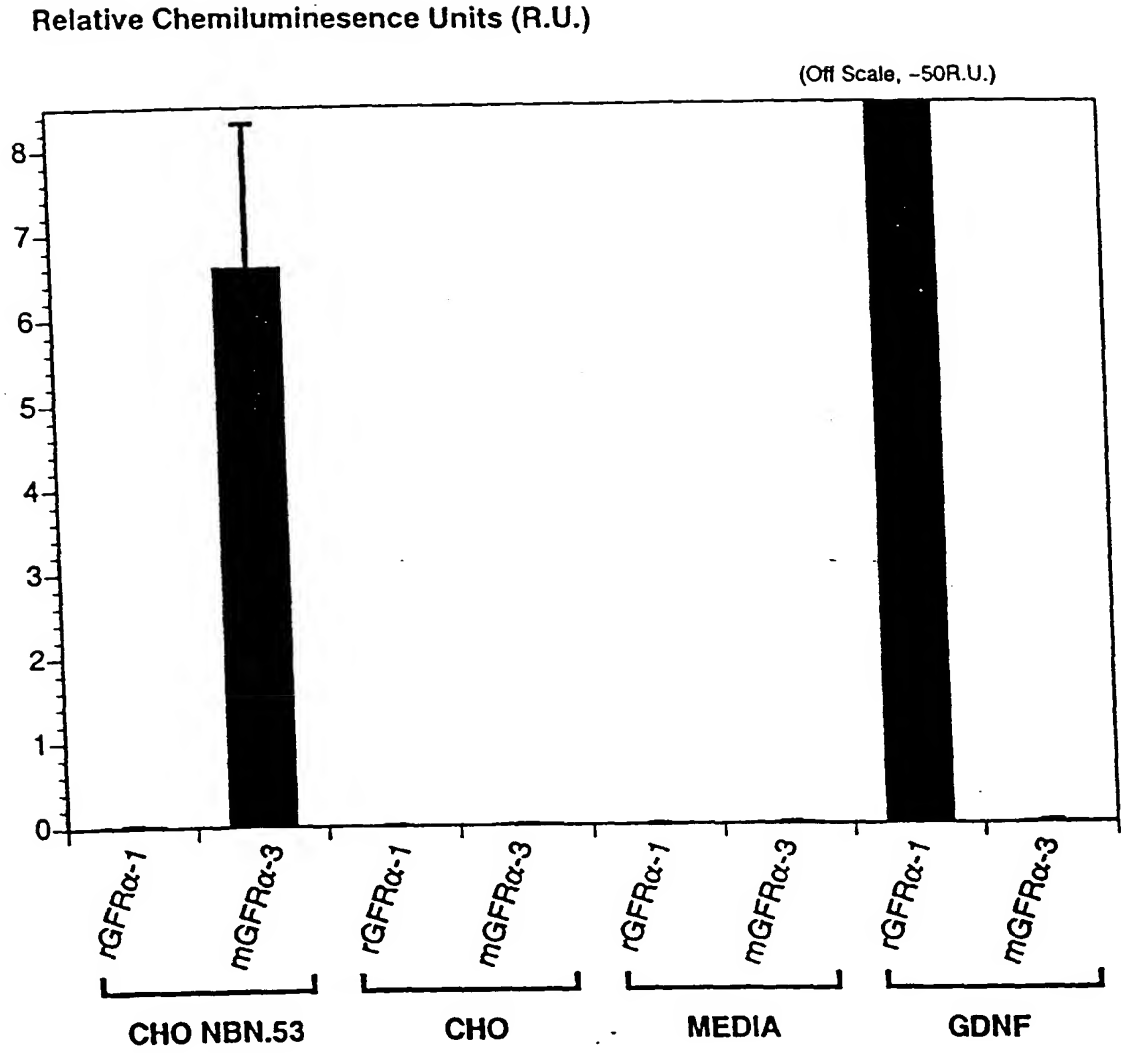
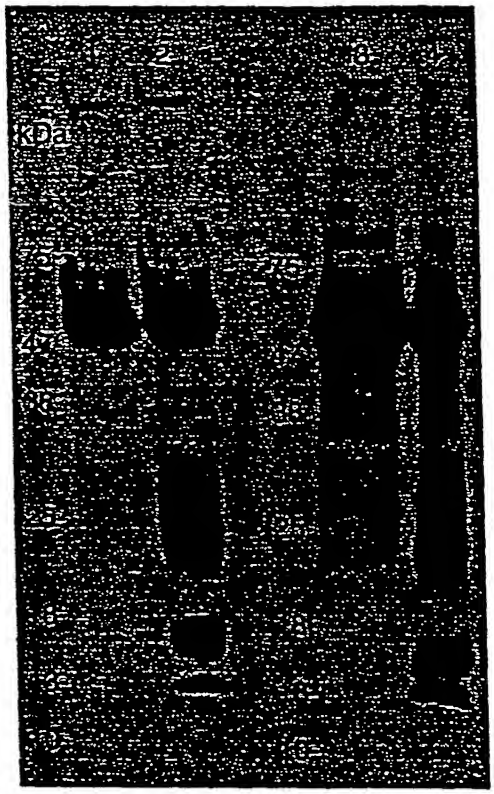
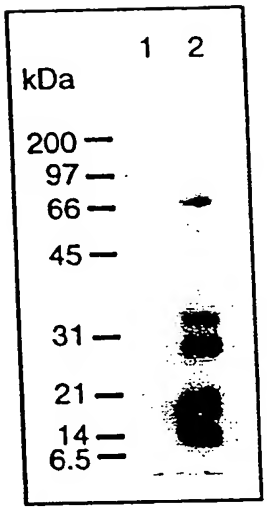

Relative Chemiluminesence Units (R.U.)
(Off Scale, -50R.U.)
8
7
6
5
4
3
2
1
0
rGFRα-1
mGFRα-3
rGFRα-1
mGFRα-3
rGFRα-1
mGFRα-3
rGFRα-1
mGFRα-3
CHO NBN.53
CHO
MEDIA
GDNF

Fig. 11



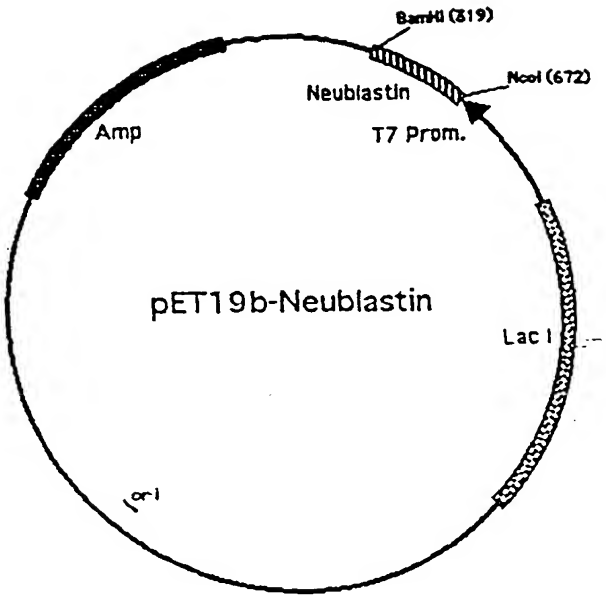
1. Control medium stained with R30 anti-peptide antibody
2. Neublastin containing conditioned medium stained with R30 anti-peptide antibody
3. Control medium stained with R31 anti-peptide antibody
4. Neublastin containing conditioned medium stained with R31 anti-peptide antibody

Fig. 12



Extraction of neublastin by affinity-binding on RETL3-Ig
Lane 1: bound from CHO control conditioned media
Lane 2: bound from neublastin overexpressing CHO conditioned media

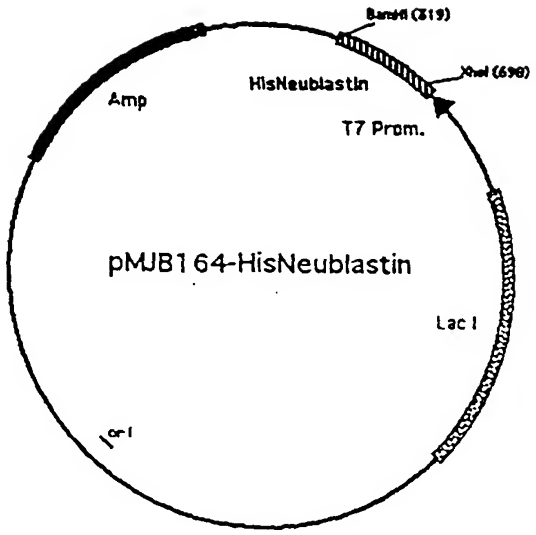
Fig. 13



Neublastin Syngene

```
      NcoI (318)
316  TACCATGGCT GGAGGACCGG GATCTCGTGC TCGTGCAGCA GGAGCACGTG GCTGTCGTCT
     ATGGTACCGA CCTCCTGGCC CTAGAGCACG AGCACGTCGT CCTCGTGCAC CGACAGCAGA
       1 M A   G G P   G S R A   R A A   G A R   G C R L

376  GCGTTCTCAA CTAGTGCCGG TGCGTGCACT CGGACTGGGA CACCGTTCCG ACGAACTAGT
     CGCAAGAGTT GATCACGGCC ACGCACGTGA GCCTGACCCT GTGGCAAGGC TGCTTGATCA
      19 R S Q   L V P   V R A L   G L G   H R S   D E L V

436  ACGTTTTCGT TTTTGTTCAG GATCTTGTCG TCGTGCACGT TCTCCGCATG ATCTATCTCT
     TGCAAAAGCA AAAACAAGTC CTAGAACAGC AGCACGTGCA AGAGGCGTAC TAGATAGAGA
      39 R F R   F C S   G S C R   R A R   S P H   D L S L

496  AGCATCTCTA CTAGGAGCCG GAGCACTAAG ACCGCCGCCG GGATCTAGAC CTGTATCTCA
     TCGTAGAGAT GATCCTCGGC CTCGTGATTC TGGCGGCGGC CCTAGATCTG GACATAGAGT
      59 A S L   L G A   G A L R   P P P   G S R   P V S Q

556  ACCTTGTTGT AGACCTACTA GATACGAAGC AGTATCTTTC ATGGACGTAA ACTCTACATG
     TGGAACAACA TCTGGATGAT CTATGCTTCG TCATAGAAAG TACCTGCATT TGAGATGTAC
      79 P C C   R P T   R Y E A   V S F   M D V   N S T W

                                                      BamHI (671)
616  GAGAACCGTA GATAGACTAT CTGCAACCGC ATGTGGCTGT CTAGGATGAT AATAGGGATC
     CTCTTGGCAT CTATCTGATA GACGTTGGCG TACACCGACA GATCCTACTA TTATCCCTAG
      99 R T V   D R L   S A T A   C G C   L G •   • •

676  CGGCT
     GCCGA
```

Fig. 14



HisNeublastin

Xhol (340)

```
301  TACCATGGGC CATCATCATC ATCATCATCA TCATCATCAC TCGAGCGGCC ATATCGACGA
     ATGGTACCCG GTAGTAGTAG TAGTAGTAGT AGTAGTAGTG AGCTCGCCGG TATAGCTGCT
       1▶ M  G  H  H  H  H  H  H  H  H  H  H  S  S  G  H  I  D  D

361  CGACGACAAG GCTGGAGGAC CGGGATCTCG TGCTCGTGCA GCAGGAGCAC GTGGCTGTCG
     GCTGCTGTTC CGACCTCCTG GCCCTAGAGC ACGAGCACGT CGTCCTCGTG CACCGACAGC
      19▶ D  D  K  A  G  G  P  G  S  R  A  R  A  A  G  A  R  G  C  R

421  TCTGCGTTCT CAACTAGTGC CGGTGCGTGC ACTCGGACTG GGACACCGTT CCGACGAACT
     AGACGCAAGA GTTGATCACG GCCACGCACG TGAGCCTGAC CCTGTGGCAA GGCTGCTTGA
      39▶ L  R  S  Q  L  V  P  V  R  A  L  G  L  G  H  R  S  D  E  L

481  AGTACGTTTT CGTTTTTGTT CAGGATCTTG TCGTCGTGCA CGTTCTCCGC ATGATCTATC
     TCATGCAAAA GCAAAAACAA GTCCTAGAAC AGCAGCACGT GCAAGAGGCG TACTAGATAG
      59▶ V  R  F  R  F  C  S  G  S  C  R  R  A  R  S  P  H  D  L  S

541  TCTAGCATCT CTACTAGGAG CCGGAGCACT AAGACCGCCG CCGGGATCTA GACCTGTATC
     AGATCGTAGA GATGATCCTC GGCCTCGTGA TTCTGGCGGC GGCCCTAGAT CTGGACATAG
      79▶ L  A  S  L  L  G  A  G  A  L  R  P  P  P  G  S  R  P  V  S

601  TCAACCTTGT TGTAGACCTA CTAGATACGA AGCAGTATCT TTCATGGACG TAAACTCTAC
     AGTTGGAACA ACATCTGGAT GATCTATGCT TCGTCATAGA AAGTACCTGC ATTTGAGATG
      99▶ Q  P  C  C  R  P  T  R  Y  E  A  V  S  F  M  D  V  N  S  T

                                                          BamHI (719)
661  ATGGAGAACC GTAGATAGAC TATCTGCAAC CGCATGTGGC TGTCTAGGAT GATAATAGGG
     TACCTCTTGG CATCTATCTG ATAGACGTTG GCGTACACCG ACAGATCCTA CTATTATCCC
     119▶ W  R  T  V  D  R  L  S  A  T  A  C  G  C  L  G  •  •

721  ATCCGGCTGC TAACAAAGCC CG
     TAGGCCGACG ATTGTTTCGG GC
```

Fig. 15

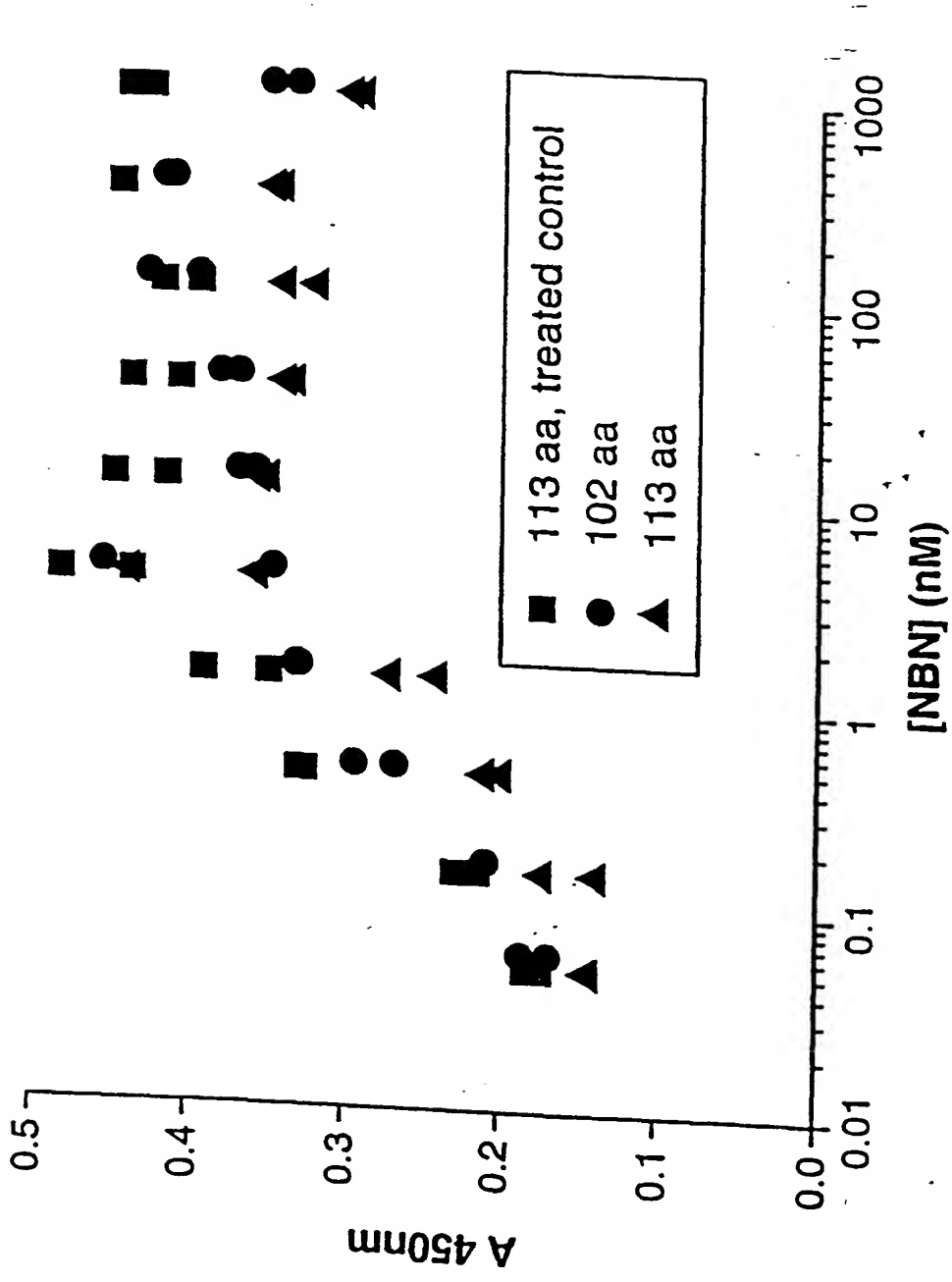

A 450nm
0.0
0.1
0.2
0.3
0.4
0.5
0.01
0.1
1
10
100
1000
[NBN] (nM)
113 aa, treated control
102 aa
113 aa

Fig. 16

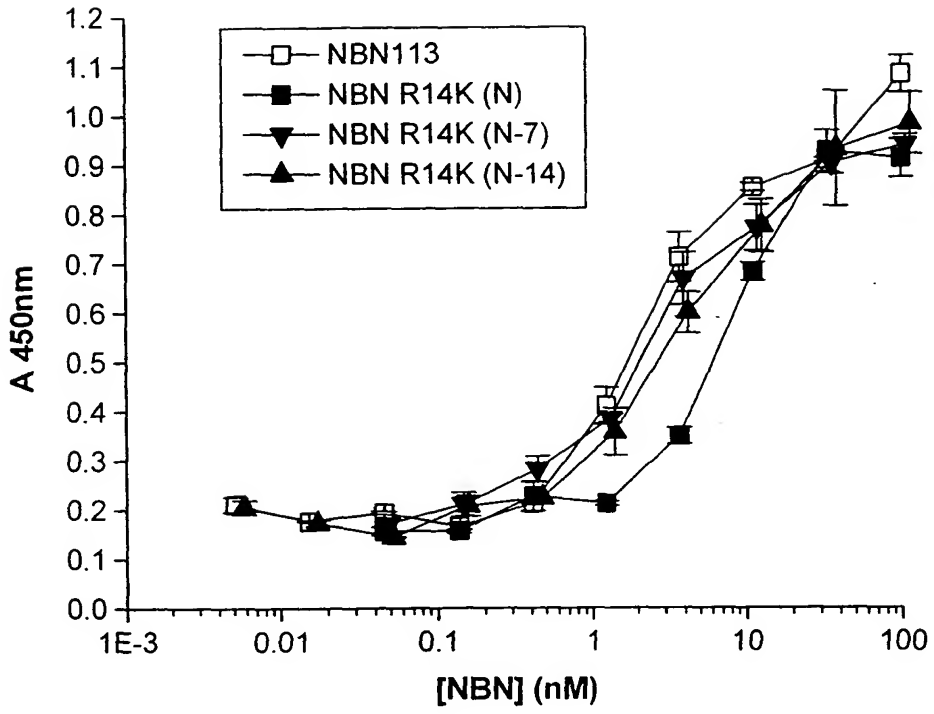

NBN113
NBN R14K (N)
NBN R14K (N-7)
NBN R14K (N-14)
A 450nm
1.2
1.1
1.0
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0.0
1E-3
0.01
0.1
1
10
100
[NBN] (nM)

FIG. 17

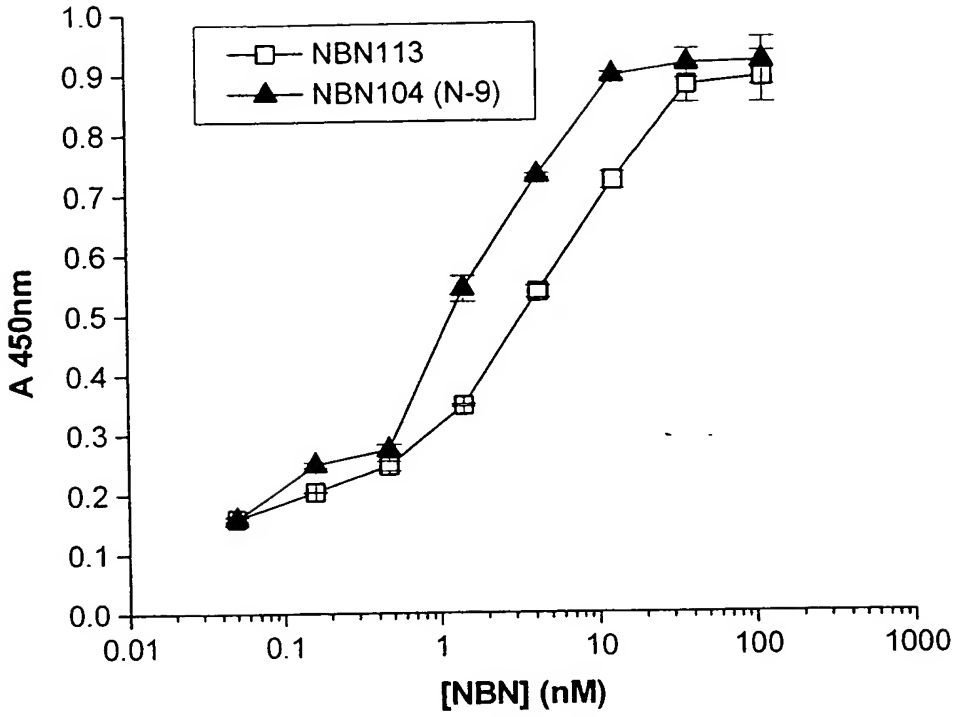

NBN113
NBN104 (N-9)
A 450nm
[NBN] (nM)
1.0
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0.0
0.01
0.1
1
10
100
1000

FIG. 18